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10/688,198	10/17/2003	Gerardo Zapata	ABGENIX.057A	6664

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EXAMINER

BRISTOL, LYNN ANNE

ART UNIT	PAPER NUMBER
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1643

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ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/688,198	Applicant(s) ZAPATA, GERARDO	
	Examiner Lynn Bristol	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 13-25 is/are pending in the application.
- 4a) Of the above claim(s) 8 and 9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 10, 11 and 13-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-11 and 13-25 are all the pending claims for this application.
2. Claim 1 was amended and Claim 12 cancelled in the Response of 5/16/07.
3. Claims 8 and 9 are withdrawn from examination. Applicant's comments regarding the withdrawal of the claims from examination in the Response of 5/16/07 on p. 5, ¶2 are acknowledged.
4. Claims 1-7, 10, 11 and 13-25 are all the pending claims under examination.
5. Applicants amendments to the claims have necessitated new grounds for rejection. This action is FINAL.

Withdrawal of Rejections

35 USC § 112- second paragraph

6. The rejection of Claim 1 (and dependent claims 2, 6-15) under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation "adjusting the conditions of the cell media" is withdrawn and moot for cancelled Claim 12 and is withdrawn for Claims 1, 2, 6-11 and 13-15 in view of amended claim 1.

Applicant's arguments filed on p. 5, ¶3 in the Response of 5/16/07 have been fully considered and are found persuasive. Applicants allege "...amended claim 1 now recites "wherein the adjusted conditions are selected from the group consisting of temperature conditions and pH conditions" which clarifies the term "adjusting the conditions of the cell media."

7. The rejection of Claims 1-18 for the recitation "endogenous enzyme" in Claim 1 because it is unclear where an "endogenous enzyme" is located for targeted activation is withdrawn and moot for cancelled Claim 12 and is withdrawn for Claims 1-11 and 13-18 in view of amended Claim 1.

Applicant's arguments filed on p. 6, ¶2 in the Response of 5/16/07 have been fully considered and are found persuasive. Applicants allege "amended Claim 1 recites at least one endogenous enzyme in said cell media" because the amendment clarifies where the endogenous enzyme is located.

35 USC § 112- first paragraph

Biological Deposit Requirement

8. The rejection of Claim 12 under 35 U.S.C. § 112, first paragraph, in lacking enablement for making the CHO-DG44 cell line or in establishing its commercial availability is withdrawn and moot in view of the cancelled claim. Applicant's comments in the Response of 5/16/07 on p. 6, ¶1 are acknowledged.

Enablement

9. The rejection of Claims 12 under 35 U.S.C. 112, first paragraph, because the specification, is lacking in enablement for performing the method invention of enzymatically digesting an antibody in a culture medium is withdrawn and moot in view of the cancelled claim.

Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. The rejection of Claims 19, 20 and 22-25 for the recitation "activating endogenous aspartyl enzyme activity" in Claim 19 because it is unclear what is meant by "activating" is maintained.

First, Applicants refer to the general support in the specification in the Response of 5/16/07 on p. 6, ¶4 where the specification teaches examples of enzymes that could be used to digest antibodies: "papain, or a similar enzyme", "pepsin, or similar enzymes", "activation of any endogenous enzyme that cleaves an antibody." On p. 7, ¶2 in the Response, Applicants excerpt the enzyme digestion protocol of the instant method invention (working example and best mode) for the step-wise adjustments to the pH and temperature for activating or inactivating the aspartyl protease, cysteinyl protease or the combination in the culture media.

In response to applicant's argument that the scope of the claims are definite and the metes and bounds are clearly defined, it is noted that the features upon which applicant relies (i.e., step-wise adjustments to the pH and temperature) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

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Second, Applicants' allege "One of ordinary skill would also understand...that other techniques (such as setting the conditions to other temperature and/or pH levels) could also be used, depending on the enzymes and/or antibodies" (p. 7, ¶3 of the Response of 5/16/07).

The Examiner submits that one skilled in the art could not determine what the metes and bounds of the invention are based on the instant claim scope in view of Applicants explanation for what is already known in this field of art. Further, and pursuant to MPEP 2144.03, "ordinarily there must be some form of evidence in the record to support an assertion of common knowledge."

For all these reasons, the rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. The rejection of Claims 1-11 and 13-25 under 35 U.S.C. 112, first paragraph, because the specification, in lacking enablement for performing the method invention of enzymatically digesting an antibody in a culture medium is maintained for reasons of record and as set forth hereinafter.

The amendment of Claim 1 to recite that the endogenous enzyme is "in said cell media" and "wherein adjusted conditions are selected from the group consisting of temperature conditions and pH conditions" does not overcome the rejection (of Claims 1-11 and 13-18) because the specification is not enabling for performing the method of

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either adjusting the temperature to just any degree or adjusting the pH to just any amount or in performing the steps in any order or manner, when instead, the specification discloses a precise, step-wise order in which the method is to be performed.

a. The specification is enabling for a method of generating antibody fragments according to the method steps of clarifying the conditioned media, stabilizing the temperature at 37°C, and adjusting the pH to about 3.5 to activate endogenous enzymes for cleaving Ig molecules

b. Applicants arguments on pp. 7, ¶4 to p. 8, ¶2 in the Response of 5/16/07 have been considered but are not found persuasive. Applicants recite the passage from the specification cited in the Office Action of 12/21/06 and allege that because Claim 1 has been amended to recite "wherein the adjusted conditions are selected from the group consisting of temperature conditions and pH conditions" that the claims are now enabled. Further, Applicants admission on the record "that not all enzymes are the same, and that reasonable experimentation will allow such person to determine the optimal conditions for such different enzymes, and thus use the present invention within the scope of the claims."

The Examiner resubmits that the specification does not enable any adjustment to the cell media comprising temperature adjustment and/or pH adjustment in any combination or in any order to specifically activate or deactivate a specific class of protease enzyme(s) without affecting the state of activation for other known or yet to be discovered enzymes that are endogenous to the cell medium so that one of skill in the

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art could *specifically and reproducibly* generate antibody binding fragments which retained their antigen binding capability.

Thus it not apparent how the instant broadly claimed invention is enabled based the disclosure in the specification at the time of application filing.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-11 and 13-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 1-11 and 13-18 are indefinite for the recitation "said conditions" in line 8 of Claim 1 because there is no antecedent basis for the phrase in Claim 1. Applicants have amended Claim 1 to recite "the adjusted conditions", "temperature conditions" and "pH conditions", therefore it is not clear what conditions are being referred to.

b) Claim 3 is indefinite for the recitation "the temperature" because there is no antecedent basis for the limitation in the claim or in Claim 1 from which it depends. Claim 1 is drawn to "temperature conditions".

c) Claims 4, 5, 16 and 17 are indefinite for the recitation "the pH" in Claims 4, 5 and 17 and the recitation "pH" in Claim 16 because there is no antecedent basis for the

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limitation in the claims or in Claim 1 from which they depend. Claim 1 is drawn to "pH conditions".

d) Claims 13-15 are indefinite as being drawn to "a protein-free media" (Claim 13), "a peptone source" (Claim 14) and "a CD-CHO media" (Claim 15) because the claims depend from claim 1 which requires a protein-containing media (i.e., containing endogenous enzymes) whereas Claims 13 and 15 specifically require that the media is protein-free. A CD-CHO media sold by GIBCO™ contains no proteins or peptides (see attached data sheet pp. 1-3). The "peptone source" of Claim 14 would presumably only contain peptides and amino acids derived from casein. A peptone source sold by Sigma-Aldrich does not disclose how the preparation was made, but the attached data sheet (pp. 1-3) indicates the contents would presumably not contain whole enzymes. Thus it is not understood how the method invention can be practiced in the absence of endogenous enzymes in the cell media.

Conclusion

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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